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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,690	10/16/2003	Michael Hale	VPI/00-127 CON DIV US	7672

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EXAMINER	
SOLOLA, TAOFIQ A	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/686,690	HALE ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1,4-9 and 12-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1,4-9 and 12-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1, 4-9, 12-25, are pending in this application.
Claims 2-3, 10-11, 26-27, are canceled.

DETAILED ACTION

Election/Restriction

The Markush group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds(or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. For these reasons provided below, restriction of the compounds of formula I is required under 35 U.S.C. 121:

In accordance with the decisions in ***In re Harnisch***, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and ***Ex parte Hozumi***, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 U.S.C. 103.

An election of a single compound (or set of compounds) is required including an exact definition of each substitution on the base molecule (Formula I), wherein a single member at each substituent group or moiety is selected. For example, if a base molecule has a substituent group R1, wherein R1 is recited to be any one of H, OH, COOH, aryl, alkoxy, halogen, amino,

etc., then applicant must select a single substituent of R1, for example OH or aryl, and each subsequent variable position. Applicant must elect one representative for R1, R2, and T.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.

Rationale Establishing Patentable Distinctiveness Within Each Group

Each Set of compound is directed to or involves the use or making of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over either of the other inventions, i.e. they are patentable over each other. Chemical structures, which are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holdings of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails

to suggest a function of a claimed compound would have been expected from a similar structure.

In addition, because of the plethora of classes and subclasses in each of the compounds of formula I, a serious burden is imposed on the examiner to perform a complete search of the defined areas. Therefore, for reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden in the examination of this application.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone call with Govindaswamy Nandakumar on 6/4/04 a provisional election was made to prosecute the invention of formula I, wherein T is a bond, R2 is phenyl or naphthyl, without traversal. Affirmation of this election must be made by applicant in replying to this Office action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-25, are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for all the diseases listed in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with claims 19-25. The inhibition of or treating any or all diseases related to ERK, JAK, JNK, Aurora, GSK, KDR or AKT (claims 16-18) is not patentable without specific diseases (utility). Applicant must set forth specific utilities in claim 16-18, which have adequate support in the specification.

The asserted utilities are not believable on their face. There is no known compound for treating all the various forms of cancer or all the diseases listed in the claims, and the specification does not provide sufficient enabling disclosure for the claimed utilities.

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988):

1) Breadth of claims.

2) Nature of invention.

3) State of prior art.

4) Level of ordinary skill in the art.

5) Level predictability in the art.

6) Amount of direction and guidance provided by the inventor.

7) Existence of working examples.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breath of the claimed invention involve the use of compounds of formulae I . The nature of the invention is in the field of medicinal chemistry wherein applicant is claiming the

methods of use of the compounds for the treatment of all forms of cardiovascular diseases, all forms of cancer and all other diseases listed in claims 19-25.

The state of the prior art is what prior art knows about the nature of the invention. There is no known prior art claiming the treatment of all forms of cardiovascular diseases, all forms of cancer and the other diseases listed in claims 19-25. The level of ordinary skill in the art is high but not in the art of treating all these various diseases with a sing drug. The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. The lower the predictability, the higher the direction and guidance that must be provided by applicant. In the instant invention the predictability is very low and consequently, the need for higher levels of direction and guidance by applicant. However, the amount of direction and guidance provided by applicant is limited to assays involving: 1) Inhibition of KDR (example 7). There is no conclusive evidence in the specification that Examples 1-6 were actually done as these examples are referred to in the specification "as may be screened" with the instant compounds. There are a vast number of conditions associated with all the claimed utility and applicant does not provide support for treating all of them. The various forms of all these disorders have different causative agents, involve different cellular mechanisms, and therefore have different treatment mechanisms and protocols. There is no evidence in the specification that established correlation between example 7 and all the various diseases listed in claims 19-25. See Ex parte Mass, 9 USPQ2d 1746, 1987. Therefore, the quantity of experimentation required to use the compounds as claimed in the instant invention, based on applicants limited disclosure would be undue burden because, one of ordinary skill in the art would have to perform significant amount of in-vivo experiments as well as additional in-vitro assays. By deleting the claims, the rejection would be overcome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 7, 9, 12, 14, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The compounds of claims 7 and 12, are enclosed individually in table 1 and 2 respectively, thus render the claims indefinite. By removing the tables and list the compounds as in claim 8, the rejection would be overcome.

The terms "Q" and "R3" lacks proper antecedent bases in claim 8 from which claim depend. Also, the term "or (f)" on line 4, claim 9, is confusing. Therefore, claim 9 is indefinite. By deleting all reference to "Q" and "R3" and replacing "or (f)" with "wherein" the rejection would be overcome.

The term "manner" line 2, claim 14, is not a term of the art, is not clear and therefore renders the claim indefinite. Also, claim 14 is a substantial duplicate of claim 13. Formulation in a pharmaceutical acceptable "manner" is inherent in the composition of claim 13. By deleting claim 14 the rejection would be overcome.

Allowable subject Matter

To place all the claims in condition for allowance, the compound claims must be amended to recite T is a bond and R2 is phenyl or naphthyl.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD, JD, whose telephone number is (703) 308-4690.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (703) 308-4532. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

TAOFIQ SOLOLA
PRIMARY EXAMINER
Group 1626

June 28, 2004